Claims

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1. A process for preparing a compound of formula (I)

(I)

where R^4 and R^5 are independently selected from hydrogen, halo, nitro, cyano, hydroxy, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, ureido, $C_{1\text{-}6}$ alkyl, $C_{2\text{-}6}$ alkenyl, $C_{2\text{-}6}$ alkynyl, $C_{1\text{-}6}$ alkoxy, $C_{1\text{-}6}$ alkanoyl,

- 10 C₁₋₆alkanoyloxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, N-(C-₁₋₆alkyl)carbamoyl, N,N-(C₁₋₆alkyl)₂carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C-₁₋₆alkoxycarbonyl, C₁₋₆alkoxycarbonylamino, N-(C₁₋₆alkyl)sulphamoyl, N,N-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino and C₁₋₆alkylsulphonyl-N-(C₁₋₆alkyl)amino; and R⁶ is hydrogen or a protecting group,
- 15 which process comprises cyclisation of a compound of formula (II)

where R^4 , R^5 and R^6 are as defined in relation to formula (I), and R^7 is a nitrogen protecting group, and removing the group R^7 , and thereafter if desired, removing any protecting group R^6 .

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2. A method according to claim 1 wherein R⁷ is a group of sub-formula (i)

(i)

where R^8 is a straight chain alkyl group of from 1 to 6 carbon atoms.

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3. A process according to claim 1 or claim 2 wherein R^4 and R^5 are independently selected from hydrogen, halo, nitro, cyano, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy, carboxy, carbamoyl, sulphamoyl, ureido, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkanoyl and C_{1-6} alkanoyloxy.

4. A compound of formula (II) as defined in claim 1.

5. A process for preparing a compound according to claim 4 which comprises reacting a compound of formula (III)

(III)

where R⁴ and R⁵ are as defined in relation to formula (I), and R¹² is a directing nitrogen protecting group, with a compound of formula (IV)

$$(R^7)_2O$$

(IV)

15 where R⁷ is as defined above, under acidic conditions.

- 6. A compound of formula (III) as defined in claim 5.
- 7. A process for preparing a compound according to claim 6 which comprises reacting a 20 compound of formula (V)

(V

where R^4 and R^5 are as defined above in claim 1 and R^{12} is as defined in relation to formula (III), with a compound of formula (VI)

LCH₂COOR⁶

(VI)

where L is a leaving group.

- 5 8. A compound of formula (V) as defined in claim 7.
 - 9. A process for preparing a compound according to claim 8 which comprises reacting a compound of formula (VII)

where R⁴ and R⁵ are as defined in claim 1 and R¹² is as defined in relation to formula (III), with a lithiating agent, such as N-butyl lithium, and subsequently with a formylating agent, such as a compound of formula (VIII)

(AIII)

where R⁹ and R¹⁰ are alkyl groups and in particular lower alkyl groups of 1 to 4 carbon atoms, such as methyl.

- 10. A compound of formula (VII) as defined in claim 9.
- 11. A process for preparing a compound according to claim 10 which comprises subjecting a compound of formula (IX)

$$R^{\frac{4}{5}}$$
 CO_2H

where R⁴ and R⁵ are as defined above in relation to formula (I), to a Curtius rearrangement reaction, in the presence of an alcohol of formula R¹²OH where R¹² is as defined in claim 5.

12. A method according to claim 1, for the production of a compound of formula (I)
5 where R⁶ is hydrogen, wherein the method further comprises the step of reacting the compound of formula (I) obtained with an amine of formula (XIII),

where R¹⁴ is selected from hydrogen or C₁₋₈alkyl,

- m is an integer of from 0 to 4,
 each R¹⁵ is the same or different and is selected from hydrogen, halo, nitro, cyano, hydroxy,
 amino, carboxy, carbamoyl, mercapto, sulphamoyl, ureido, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl,
 C₁₋₆alkoxy, C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino,
 C₁₋₆alkanoylamino, N-(C₁₋₆alkyl)carbamoyl, N,N-(C₁₋₄alkyl)₂carbamoyl, C₁₋₆alkylS(O)_a
- wherein a is 0 to 2, C₁₋₆alkoxycarbonyl, C₁₋₆alkoxycarbonylamino, N-(C₁₋₆alkyl)sulphamoyl, N,N-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino, C₁₋₆alkylsulphonyl-N-(C₁₋₆alkyl)amino, C₃₋₈cycloalkyl, C₃₋₈cycloalkylC₁₋₆alkyl, aryl, arylC₁₋₆alkyl, heterocyclic group and (heterocyclic group)C₁₋₆alkyl; wherein R¹ may be optionally substituted on carbon by one or more groups selected from P and wherein if said
- 20 heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R;

each R¹⁶ is the same or different and is selected from is hydrogen or C₁₋₆alkyl;

R¹⁷ is selected from hydrogen, halo, nitro, cyano, hydroxy, fluoromethyl,
difluoromethyl, trifluoromethyl, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto,

25 sulphamoyl, ureido, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl,
C₁₋₆alkanoyloxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino,
N-(C₁₋₆alkyl)carbamoyl, N,N-(C₁₋₄alkyl)₂carbamoyl, N-(C₁₋₆alkyl)-N-(C₁₋₆alkoxy)carbamoyl,
C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl, C₁₋₆alkoxycarbonylamino,
N-(C₁₋₆alkyl)sulphamoyl, N,N-(C₁₋₆alkyl)₂sulphamoyl, sulphamoylamino,

30 $N-(C_{1-6}alkyl)$ sulphamoylamino, $N,N-(C_{1-6}alkyl)$ sulphamoylamino, $C_{1-6}alkyl$ sulphamoylamino,

C₁₋₆alkylsulphonylaminocarbonyl, C₁₋₆alkylsulphonyl-*N*-(C₁₋₆alkyl)amino and a group -E-F-G-H;

wherein E and G are independently selected from a direct bond, -O-, -S-, -SO-, -SO₂-, -OC(O)-, -C(O)O-, -C(O)-, -NR^a-, -NR^aC(O)-, -C(O)NR^a-, -SO₂NR^a-, -NR^aSO₂-,

5 -NR^aC(O)NR^b-, -OC(O)NR^a-, -NR^aC(O)O-, -NR^aSO₂NR^b-, -SO₂NR^aC(O)- and -C(O)NR^aSO₂-; wherein R^a and R^b are independently selected from hydrogen or C₁₋₆alkyl which is optionally substituted by a group V;

F is C₁₋₆alkylene optionally substituted by one or more Q or a direct bond;

H is selected from aryl, C₃₋₈cycloalkyl and heterocyclic group; wherein H may be optionally substituted on carbon by one or more groups selected from S and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from T;

- P, S and Q are independently selected from halo, nitro, cyano, hydroxy, trifluoromethyl, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, ureido,
- 15 C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, N-(C₁₋₆alkyl)carbamoyl, N,N-(C₁₋₆alkyl)₂carbamoyl, N-(C₁₋₆alkyl)-N-(C₁₋₆alkoxy)carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl, C₁₋₆alkoxycarbonylamino, N-(C₁₋₆alkyl)₂sulphamoyl, N,N-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkylsulphonylamino,
- 20 C₁₋₆alkylsulphonyl-N-(C₁₋₆alkyl)amino, C₃₋₈cycloalkyl, aryl and heterocyclic group; wherein P, S and Q may be optionally and independently substituted on carbon by one or more groups selected from V and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from U;

V is selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, carboxy, carbamoyl, mercapto, sulphamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, N-methyl-N-ethylamino, acetylamino, N-methylcarbamoyl, N-ethylcarbamoyl, N,N-dimethylcarbamoyl, N,N-diethylcarbamoyl, N-methyl-N-ethylcarbamoyl, methylthio, ethylthio, methylsulphinyl, ethylsulphinyl, mesyl, ethylsulphonyl, methoxycarbonyl, ethoxycarbonyl,

30 N-methylsulphamoyl, N-ethylsulphamoyl, N,N-dimethylsulphamoyl, N,N-diethylsulphamoyl, N-methyl-N-ethylsulphamoyl, morpholino, morpholinocarbonyl, N- benzylcarbamoyl, and 4-hydroxypiperidinocarbonyl;

R, T and U are independently selected from C₁₋₄alkyl, C₁₋₄alkanoyl, C₁₋₄alkylsulphonyl, C₁₋₄alkoxycarbonyl, carbamoyl, N-(C₁₋₄alkyl)carbamoyl, N,N-(C₁₋₄alkyl)carbamoyl, phenyl, benzyl, benzyloxycarbonyl, benzoyl and phenylsulphonyl wherein R, T and U may be optionally and independently substituted on carbon by one or more groups selected from V; to produce a compound of formula (XIV)

$$\begin{array}{c|c}
R^4 & H & R^{14} \\
R^5 & O & R^{15} \\
\hline
(XIV)
\end{array}$$

where R⁴, R⁵, R¹⁵, R¹⁶, R¹⁷ and m are as defined above, or a pharmaceutically acceptable salt 10 or an *in vivo* hydrolysable ester thereof.